H2

Claim 41: An isolated cDNA molecule which encodes a tumor rejection antigen precursor expressed in melanoma cells, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 13, 14 or 15 at 0.1XSSC, 0.1%SDS, for 30 minutes at 65°C.

REMARKS

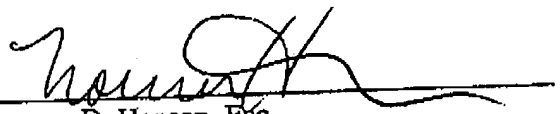
Claims 39 & 41 are amended. A "Show of Changes" is attached. In claim 39 "fragment of a" was added to modify tumor rejection antigen precursor, and in claim 41, "cDNA" replaces "nucleic acid." The result is that the claims parallel the claims of U.S. Patent No. 6,498,021, a copy of which is attached.

It is believed that since claims 38, 39 and 41 are no longer identical, the issues related to claims 50, 53 & 56 are moot. Claims 59 & 62 have been cancelled, rendering these claims moot.

Allowance is now believed proper.

Respectfully submitted,

FULBRIGHT & JAWORSKI, L.L.P.



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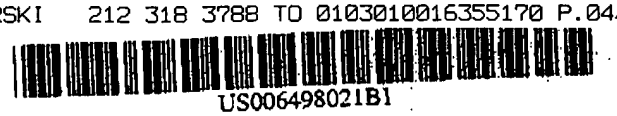

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(12) **United States Patent**
Guagler

(10) **Patent No.: US 6,498,021 B1**
(45) **Date of Patent: Dec. 24, 2002**

(54) **ISOLATED NUCLEIC ACID MOLECULES CODING FOR TUMOR REJECTION ANTIGEN PRECURSOR MAGE-8 AND USES THEREOF**

(75) Inventor: **Béatrice Guagler**, Brussels (BE)

(73) Assignee: **Ludwig Institute for Cancer Research**, New York, NY (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 10 days.

(21) Appl. No.: **09/583,850**

(22) Filed: **May 31, 2000**

Related U.S. Application Data

(60) Division of application No. 09/404,026, filed on Sep. 23, 1999, which is a division of application No. 08/967,727, filed on Nov. 12, 1997, now Pat. No. 6,025,474, which is a division of application No. 08/037,230, filed on Mar. 26, 1993, now Pat. No. 6,235,525, which is a continuation-in-part of application No. PCT/US92/04354, filed on May 22, 1992, which is a continuation-in-part of application No. 07/807,043, filed on Dec. 12, 1991, now Pat. No. 5,342,774, which is a continuation-in-part of application No. 07/764,365, filed on Sep. 23, 1991, which is a continuation-in-part of application No. 07/728,838, filed on Jul. 9, 1991, which is a continuation-in-part of application No. 07/705,702, filed on May 23, 1991, now abandoned.

(51) **Int. Cl.**[7] **C12P 21/06**; C07K 1/00; C07K 14/00; C07K 17/00; C07H 5/04

(52) **U.S. Cl.** 435/69.1; 435/69.3; 435/184.1; 435/185.1; 435/325; 435/363; 435/366; 530/350; 536/1; 536/18.7; 536/22.1; 536/23.1; 536/23.5; 536/24.1

(58) **Field of Search** 536/1, 18.7, 22.1, 536/23.1, 23.5, 24.1; 435/325, 363, 366, 184.1, 185.1, 69.1, 69.3; 530/350

(56) **References Cited**

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Reiger and Green. Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, pp. 17–18,1976.*

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Assistant Examiner—Alana M. Harris
(74) *Attorney, Agent, or Firm*—Fulbright & Jaworski LLP

(57) **ABSTRACT**

The invention relates to nucleic acid molecules which code for the tumor rejection antigen precursor MAGE-8. Also disclosed are vectors, cell lines, and so forth, which utilize the nucleic acid molecule, and optionally, molecules coding for human leukocyte antigen HLA-A1. Use of these materials in therapeutic and diagnostic contexts are also a part of the invention.

30 Claims, 17 Drawing Sheets

-continued

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acids
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

Glu Ala Asp Pro Thr Gly His Ser Tyr
5

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ACTCAGCTCC TCCCAGATTT 20

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

GAAGAGGAGG GGCCAAG 17

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

TCTTGTATCC TGGAGTCC 18

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

TTGCCAAGAT CTCAGGAA 18

I claim:

1. An isolated nucleic acid molecule which encodes a tumor rejection antigen precursor, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 20 at 0.1×SSC, 0.1%SDS.

2. An isolated nucleic acid molecule which encodes a fragment of a tumor rejection antigen precursor, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 20 at 0.1×SSC, 0.1%SDS.

3. An isolated nucleic acid molecule which encodes a tumor rejection antigen, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 20 at 0.1×SSC, 0.1%SDS.

4. An isolated cDNA molecule which encodes a tumor rejection antigen precursor, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to nucleotides 451–1156 of SEQ ID NO: 20 at 0.1×SSC, 0.1%SDS.

5. The isolated nucleic acid molecule of claim 1, wherein said nucleic acid molecule is cDNA.

6. An isolated cDNA molecule which encodes a fragment of a tumor rejection antigen precursor, wherein said fragment is processed by cell to a tumor rejection antigen, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to nucleotides 451–1156 of SEQ ID NO: 20 at 0.1×SSC, 0.1%SDS.

7. An isolated cDNA molecule which encodes a tumor rejection antigen, said tumor rejection antigen consisting of an amino acid sequence that is part of a tumor rejection antigen precursor, wherein said tumor rejection antigen precursor is encoded by a nucleic acid molecule the complementary sequence of which hybridizes to nucleotides 451–1156 SEQ ID NO: 20 at 0.1×SSC, 0.1% SDS.

8. The isolated nucleic acid molecule of claim 1, comprising SEQ ID NO: 20.

9. An expression vector comprising the isolated nucleic acid molecule of claim 5, operably linked to a promoter.

10. An expression vector comprising the isolated nucleic acid molecule of claim 6, operably linked to a promoter.

11. An expression vector comprising the isolated nucleic acid molecule of claim 7, operably linked to a promoter.

12. A host cell transformed or transfected with the isolated nucleic acid molecule of claim 1.

13. A host cell transformed or transfected with the isolated nucleic acid molecule of claim 2.

14. A host cell transformed or transfected with the isolated nucleic acid molecule of claim 3.

15. The host cell of claim 12, wherein said cell is a fibroblast.

16. The host cell of claim 13, wherein said cell is a fibroblast.

17. The host cell of claim 14, wherein said cell is a fibroblast.

18. The host cell of claim 12, wherein said cell is a mammalian cell.

19. The host cell of claim 13, wherein said cell is a mammalian cell.

20. The host cell of claim 19, wherein said cell is a mammalian cell.

21. An isolated nucleic acid molecule which encodes a tumor rejection antigen precursor encoded by nucleotides 451–1156 of SEQ ID NO: 20.

22. An isolated nucleic acid molecule which encodes a fragment of a tumor rejection antigen precursor that is encoded by nucleotides 451–1156 of SEQ ID NO: 20.

23. An isolated nucleic acid molecule which encodes a tumor rejection antigen, the amino acid sequence of which consists of an amino acid sequence that is a part of the amino acid sequence encoded by nucleotides 451–1156 of SEQ ID NO: 20.

24. The isolated nucleic acid molecule of claim 21, wherein said nucleic acid molecule is cDNA.

25. The isolated nucleic acid molecule of claim 22, wherein said molecule is cDNA.

26. The isolated nucleic acid molecule of claim 23, wherein said molecule is cDNA.

27. An isolated genomic DNA molecule which encodes a tumor rejection antigen precursor, and comprises a nucleotide sequence consisting of nucleotides 451–1156 of SEQ ID NO: 20.

28. An isolated genomic DNA molecule which encodes the tumor rejection antigen precursor encoded by the isolated genomic DNA molecule of claim 27.

29. The isolated genomic DNA molecule of claim 27, comprising the nucleotide sequence of SEQ ID NO: 20.

30. The isolated genomic DNA molecule of claim 27, consisting of the nucleotide sequence of SEQ ID NO: 20.

* * * * *

VIA FACSIMILE

I hereby certify that this correspondence is being facsimile transmitted to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 on February 6, 2003.

Fulbright & Jaworski L.L.P.

LUD-5353.5 JEL/NDH (10016355)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant	:	Beatrice GAUGLER et al.
Serial No.	:	09/579,543
Filed	:	May 26, 2000
For	:	ISOLATED NUCLEIC ACID MOLECULES CODING FOR TUMOR REJECTION ANTIGEN PRECURSOR MAGE-4 AND 41 AND USES THEREOF
Art Unit	:	1642
Examiner	:	Alana Harris

February 6, 2003

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

SHOWING OF CHANGES

Claim 39: An isolated nucleic acid molecule which encodes a fragment of a tumor rejection antigen precursor expressed in melanoma cells, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 13, 14 or 15 at 0.1XSSC, 0.1%SDS for 30 minutes, at 65°C.

Claim 41: An isolated [nucleic acid] cDNA molecule which encodes a tumor rejection antigen precursor expressed in melanoma cells, wherein the complementary sequence of said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 13, 14 or 15 at 0.1XSSC, 0.1%SDS, for 30 minutes at 65°C.

Respectfully submitted,

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